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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,354	12/22/2004	Robert J. Hariri	9516-059-999	6502

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EXAMINER	
BRISTOL, LYNN ANNE	
ART UNIT	**PAPER NUMBER**
1643	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,354	HARIRI ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-24 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-24 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-24 are all the pending claims for this 371 application and subject to lack of unity restriction/election of species requirement.

2. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

To have a general inventive concept under PCT rule 13.1, the inventions need to be linked by a special technical feature. The special technical feature that appears to link claims 1-24 is a modulator of angiogenesis which targets stem cell outgrowth of endothelial cell formation of microvessel outgrowth, and more specifically for claim 1, a method of identifying a modulator.

Lyden et al. (Nature Medicine (Nov. 2001) 7:1194-1201) discuss identifying modulators for bone-marrow derived precursor cells in tumor angiogenesis using anti-VEGFR1 and -VEGFR2 antibodies to block tumor angiogenesis and growth. Mice treated with anti- VEGFR2 had decreased vessel density and for mice treated with both anti-VEGFR1 and -VEGFR2 antibodies there was extensive necrosis and no evidence of viable capillaries and tumor growth (Fig. 6, p.1198, Col. 2- p. 1199, Col. 1). Lyden demonstrates that inhibition of VEGFR1 and VEGFR2 blocks early phases of tumor growth by blocking recruitment of VEGF-responsive BM precursors.

Mesters et al. (Blood (July 2001) 98(1):241-243) discuss targeting bone marrow microvessel formation in bone marrow from an AML patient by blocking the stem cell

factor receptor c-kit with the small molecule receptor tyrosine kinase inhibitor SU5416 (see Figure 2).

Therefore the technical feature recited in the claims is not a contribution over the prior art. Accordingly the groups set forth below are not so linked as to form a single general concept under PCT Rule 13.1.

3. In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-13, drawn to a method of identifying an angiogenesis modulator comprising culturing stem cells in the presence of a test compound suitable for endothelial cell growth, and comparing microvessel outgrowth from the stem cells between the test compound and a control.

Group II, claim(s) 14-24, drawn to a method of treating a subject having abnormal vessel growth or angiogenesis with a TNF-α inhibitor.

4. The inventions listed as Groups I and II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical feature for the following reasons: As set forth above in view of the teachings from Lyden et al. and Mesters et al. the groups are not so linked as to form a single general concept under PCT Rule 13.1 because the technical feature shared by Groups I and II is not special.

5. The methods of Groups I and II differ in the method objectives, method steps and parameters, intended populations and in the reagents used. The method of Group I does not require treating a subject to obtain a therapeutic endpoint unlike the method of

Group II. The method of Group II does not require identifying a modulatory compound against a control unlike the method of Group I. The examination of all groups would require different searches in the U.S. and foreign patent literature and the scientific literature and would require the consideration of different patentability issues. Thus Inventions of Groups I and II are separate and distinct in having different method steps, intended populations and different reagents and are patentably distinct.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Election of Species

7. Group I contains claims directed to the following patentably distinct species (stem cell culture conditions) of the claimed invention:

a. hydrocortisone

b. epidermal growth factor

c. bovine brain extract

The species of component for the stem cell culture condition are structurally and functionally different molecules. For example, hydrocortisone is a steroid, epidermal growth factor is a protein growth factor and bovine brain extract contains an undefined,

complex mixture of hormones, proteins, fatty acids, etc. It is expected that each of the species would effect stem cell differentiation through different signaling pathways with each having a different end result on stem cell differentiation. Therefore, the species are patentably distinct.

If Applicant elects Invention of Group I, Applicant is required under 35 U.S.C. 121 to further elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 11-4 and 6-13 are generic.

8. Group II contains claims directed to the following patentably distinct species (disease or condition) of the claimed invention:

a. inflammation

b. endometriosis

c. arthritis

d. atherosclerotic plaques

e. diabetic retinopathy

f. neovascular glaucoma

g. trachoma

h. corneal graft neovascularization

i. psoriasis

j. scleroderma

k. hemangioma and hypertrophic scarring

l. vascular adhesions

m. angiofibroma

The species of disease or condition associated with abnormal vessel growth are patentably distinct since they involve separate and distinct tissues, patient populations, different diagnostic symptoms and tests, and separate methods of treatment. For example, endometriosis occurs in women with symptoms such as ovarian cysts, ectopic pregnancy, Pelvic Inflammatory Disease, irritable bowel syndrome, ovarian cancer, fibroid tumours, colon cancer and appendicitis. In contrast, angiofibroma is a benign vasoformative tumor occurring almost exclusively in adolescent males and associated with symptoms such as Periodic nosebleeds, facial swelling, nasal congestion, hyponasal speech (not enough air flow through the nose) and otorrhea (draining ear). A search for any one of the other species in a commercial medical reference textbook or a disease non-profit website would reveal that any one of the respective diseases and its symptoms is distinguishable. Therefore, the species are patentably distinct.

If Applicant elects Invention of Group II, Applicant is required under 35 U.S.C. 121 to further elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, Claims 14-19 and 21-24 are generic.

9. Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim

is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER